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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/380,682	10/19/99	MOSSAKOWSKA	D 88362/107

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EXAMINER	
BRANNOCK, M	
ART UNIT	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/380,682	Applicant(s) Mossakowska
	Examiner Michael Brannock, Ph.D.	Group Art Unit 1646

☒ Responsive to communication(s) filed on *Dec 21, 2000*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is clos d** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *28-51* is/are pending in the applicat

Of the above, claim(s) *30-41, 44-48, and 51* is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *28, 29, 42, 43, 49, and 50* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☒ Claims *28-51* are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☒ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☒ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *7*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Status of Application: Claims and Amendments

1. Claims 28-51 are pending.

2. Claims 30-41, 44-48 and 51 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention, the requirement having been traversed in Paper No. 12, 12/21/00. Further, Applicant is reminded that the claims will be examined only to the extent that they read on the elected species of SEQ ID NO: 1. As no arguments were presented as to why the restriction requirement may be improper, the requirement is maintained and made FINAL.

Claim Objections

3. Claim 42 is objected to because of the following informalities: in the last paragraph of the claim, a coma is required between "affinity" and "covalently". Appropriate correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 28, 29 42, 43, 49 and 50 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for the following reasons.

a) The claims require a polypeptide of comprising short consensus repeats "as the only structurally and functionally intact SCR domains of CR1". This phrase is confusing and renders the claims indefinite for several reasons. First, it is unclear what relationship CR1 has to the claimed polypeptide, e.g. *is* the claimed polypeptide CR1 or an example of CR1 or different than CR1? Is this phrase meant to be an aside or a parenthetical statement describing CR1, but not placing any limitations on the claimed polypeptide? Second, the specification has not provided sufficient guidance to one of skill in the art to be able to unambiguously conclude what is and what is not a structurally and functionally intact SCR domain - such determination being required to establish the bounds of the claim. The description of the term "SCR" at pages 1-2 of the specification is insufficient to allow one of skill in the art to be able to unambiguously conclude what is and what is not an "SCR". Further, the words "structurally" and "functionally" are relative words and it is impossible to know what is and what is not encompassed by these terms as they are used in the claims.

b) The phrase "wherein at least one of the native amino acids is substituted" (e.g. claim 28) is indefinite because the claim set forth which polypeptide, nor which portion thereof, is considered "native".

c) The positions of the proposed amino acid substitutions are indefinite (e.g. Val at position 4, claim 28) because the claim does not put forth where the numbering is to start from, e.g. is this position 4 of the claimed polypeptide, or of CR1 or of LHR-A or of any one of the SCR domains?

d) Claims 42, 43 and 49 require "derivatives" of the recited polypeptide. The word "derivatives" renders the claims indefinite because the claims include amino acid sequences and chemical modification not actually disclosed, thereby rendering the metes and bounds of the claim unascertainable. The specification provides some examples of derivatives, however, examples are not sufficient to define the bounds of a claim. The specification does not provide guidelines for measuring the degree of "derivation" nor can the metes and bounds of the term "derivative" be ascertained when read in light of the specification. One of ordinary skill in the art, would not be reasonably apprised of the metes and bounds of the invention.

e) In claim 42, the phrase "membrane binding elements with low affinity" renders the claim indefinite because the description of the term "low affinity" at page 9 of the specification is insufficient to allow one of skill in the art to be able to unambiguously conclude what is and what is not "low affinity". The specification puts forth that elements that bind with low affinity have significant affinity with dissociation constants of greater than 1 μM, thus it is unclear what the limits of the term are, e.g. would a dissociation constant of 1 M be considered to have significant affinity and therefore low affinity?

f) In the first line of claim 42 and of 49, the phrase "that comprises in sequence" lacks antecedent bases, i.e. it is unclear whether the phrase applies to "A soluble derivative" or to "a soluble polypeptide".

g) In claim 40 the term "thermodynamic additivity" renders the claim indefinite because there is no art-recognized definition of the term and nor is the description of the term at page 8 of the specification sufficient to allow one of skill in the art to be able to unambiguously conclude what is and what is not ""thermodynamic additivity".

h) Claims 28 and 42 appear to contain improper Markush type groups, wherein the SCR is selected from SCR 1, 2, 3, *and* 4. To be proper, the claim should recite "SCR 1, 2, 3, *or* 4". Alternatively the claim could recite "selected from *the group consisting of* SCR 1, 2, 3, *and* 4".

j) It is suggested to Applicant that sequence identifiers, of the form SEQ ID NO: X, be used in the claims such that the metes and bounds of the claims can be ascertained.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 43 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification discloses a polypeptide of SEQ ID NO: 1, yet the claim encompasses polypeptide derivatives not described in the specification, i.e. those comprising membrane binding sequences identified through screening of random chemical libraries. None of these sequences meet the written description provision of 35 U.S.C. 112, first paragraph. Although one of skill in the art would reasonably predict that these sequences exist, one would not be able make useful predictions as to the positions or identities of those sequences based on the information disclosed in the specification.

With the exception of the of the polypeptide of SEQ ID NO: 1, the skilled artisan cannot envision the detailed chemical structure of the encompassed variants. Therefore, only the polypeptide of SEQ ID NO: 1, and polypeptides derivatives thereof comprising membrane binding elements taught in the specification, but not the full breadth of the claims meet the written description provision of 35 U.S.C. §112, first paragraph.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 28, 29, and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No: 5545619 in view of Hourcade et al., J. Biol. Chem. 265(2)974-980, 1990.

U.S. Patent No: 5545619 teaches a soluble polypeptide (CR1) comprising one to four short consensus repeats of the long homologous repeat A (LHR-A) and related polypeptides termed RCA polypeptides (see col 6), methods of producing mutations is said polypeptides (see col 7), and pharmaceutical compositions containing therapeutically effective amounts of same (see col. 9). By way of reference to Hourcade et al., U.S. Patent No: 5545619 discloses that amino acid sequences having the mutations recited in the instant claims are encompassed by the invention (see col. 6, lines 6-15). These mutations are disclosed by Hourcade et al., (see Figure 3), as pointed to by U.S. Patent No: 5545619. Claim 42 also requires that the polypeptide derivative comprises at least two heterologous membrane binding elements with low membrane affinity, covalently associated with the polypeptide, wherein the elements are capable of interacting independently and with thermodynamic additivity with the components of cellular membranes exposed to extracelluar fluids. The instant specification states that preferred membrane binding elements are basic amino acid sequences (see the bottom of page 9). The amino acid sequence taught by Hourcade et al. provides for at least 8 heterologous basic amino acids (arginine and lysine) relative to CR1 (see Figure 3 of Hourcade et al.).

Therefore, it would have been obvious to one of ordinary skill in the art, at the time the invention was made, with reasonable expectation of success, to produce a polypeptide having the amino acid sequence taught by Hourcade et al. when practicing the invention disclosed in U.S.

Patent No: 5545619. The motivation to do so was provided in U.S. Patent No: 5545619 wherein it was stated that the term "RCA proteins" refers to that taught by Hourcade et al. (see col. 6, lines 6-15), and that such proteins are useful in therapeutic and prophylactic contexts (see the last paragraph of col. 8).

10. Claims 43 and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No: 5545619 in view of Hourcade et al., J. Biol. Chem. 265(2)974-980, 1990, as applied to claims 28, 29, 42 and 50 above, and in further view of Clissold et al., Eur. J. Immunol. 23(2346-2352)1993 and U.S. Patent No: 5936092. Claims 43 and 49 contain the elements discussed above regarding claims 28, 29, 42 and 50, yet claims 43 and 49 also require that the polypeptide derivative comprise at least two heterologous membrane binding elements consisting of fatty acid derivatives. Claim 49 also requires that the process of constructing the polypeptide include recovering the polypeptide and, thereafter, post-transnationally modifying the polypeptide to chemically introduce the membrane binding elements.

Clissold et al. teach that the addition of a membrane binding element (glycosyl-phosphatidylinositol, GPI) to soluble CR1 increases the effectiveness of CR1 at protecting cells from complement mediated damage (see the abstract). Thus, Clissold et al. teach the concept that membrane binding elements increase the effectiveness of CR1. In the experiments of Clissold et al., there is only a single membrane binding element, and that element was added to CR1 during the expression of the polypeptide and not after recovery, as required by claim 49.

However, the conjugation of fatty acid molecules to proteins for use in directing the proteins to the membrane of cells is well known in the art. U.S. Patent No: 5936092 discloses methods of conjugating fatty acid moieties to polypeptides for after the polypeptides have been expressed and recovered (see, for example, col. 10)

Therefore, it would have been obvious to one of ordinary skill in the art, at the time the invention was made to post-transnationally modify a polypeptide, said polypeptide being taught by Patent No: 5545619 in view of Hourcade et al., as discussed above, with membrane binding elements using the methods disclosed by U.S. Patent No: 5936092. The motivation to do so was provided by Clissold et al. who teach the concept that membrane binding elements increase the effectiveness of CR1.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Brannock, Ph.D., whose telephone number is (703) 306-5876. The examiner can normally be reached on Mondays through Fridays from 8:00 a.m. to 4:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, Ph.D., can be reached at (703) 308-6564.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

David Ramo
Primary Examiner

MB

February 21, 2001